

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
23 January 2003 (23.01.2003)

PCT

(10) International Publication Number  
**WO 03/006100 A1**

(51) International Patent Classification<sup>7</sup>: **A61M 37/00**,  
36/00, B01D 61/00, 61/20, 61/30

H.; 18 Sunrise Road, Boxford, MA 01921 (US). **TREU, Dennis, M.**; 8 Twin Brook Lane, Bedford, NH 03110 (US).

(21) International Application Number: PCT/US02/22184

(22) International Filing Date: 11 July 2002 (11.07.2002)

(74) Agents: **KAPPOS, John, C.** et al.; Lyon & Lyon, LLP, 633 West Fifth Street, Suite 4700, Los Angeles, CA 90071-2066 (US).

(25) Filing Language: English

(81) Designated States (*national*): AU, CA, JP.

(26) Publication Language: English

(30) Priority Data:  
09/905,246 12 July 2001 (12.07.2001) US

(84) Designated States (*regional*): European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR).

(71) Applicant: **NXSTAGE MEDICAL, INC.** [US/US]; 439 S. Union Street, Fifth Floor, Lawrence, MA 01843 (US).

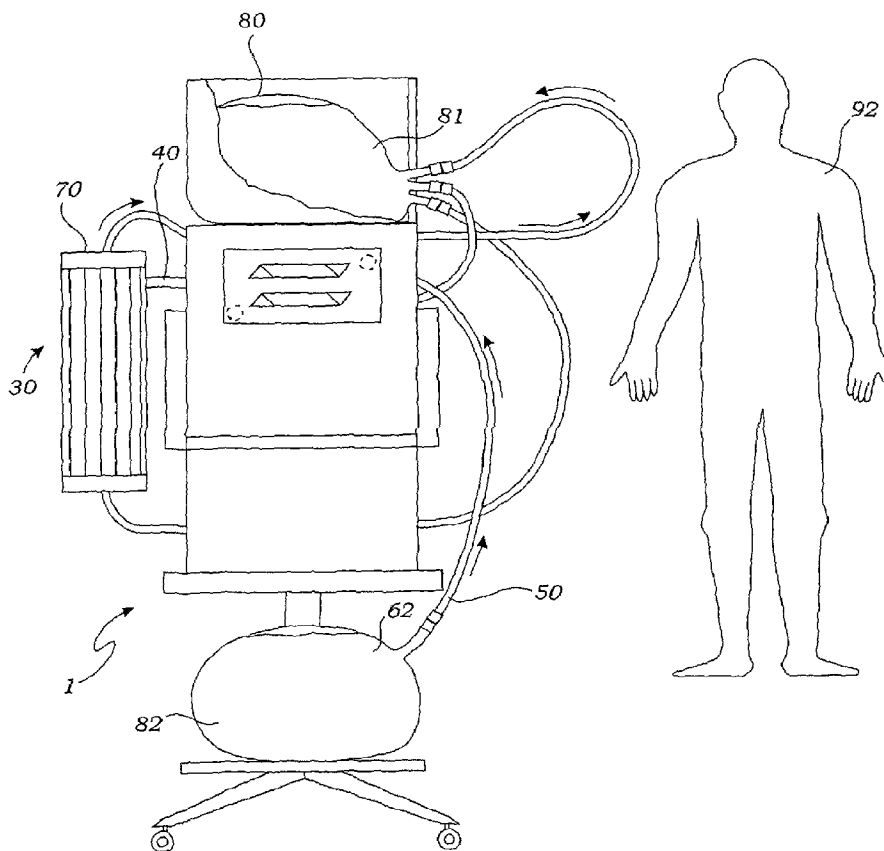
Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(72) Inventors: **BRUGGER, James, M.**; 4 Savory Street, Newburyport, MA 01950 (US). **BURBANK, Jeffrey,**

[Continued on next page]

(54) Title: DEVICES FOR STERILE-FILTERING FLUID AND METHODS OF USE



(57) Abstract: A method and device for renal replacement therapy is described. Sterile filtered solution can be subsequently used as a replacement fluid in the same unit. The devices and methods include a pump that can be reversed from its normal forward-pumping direction to sterilize a container (62) of replacement fluid (82) to produce sterile replacement fluid (81). The sterile replacement fluid (81) is captured in a fluid bag (80). Upon sterilization of the contents of the container (62), the pump switches to run in its normal forward-pumping direction. The sterile replacement fluid (81) produced by the previous process is now injected into a patient (92) to perform renal replacement therapy. The waste produced during the renal replacement therapy can be trapped in the container (62) that previously held the non-sterile solution (82).



WO 03/006100 A1



---

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## Devices For Sterile-Filtering Fluid and Methods of Use

### Field of the Invention

5 The present invention relates generally to medical devices and methods useful for batch sterile-filtering fluid prior to use as a replacement fluid in renal replacement therapies. More particularly, the devices and methods include using a filter such as a hemofilter first for sterile filtration of a replacement fluid to render the fluid sterile, followed by a renal replacement therapy that uses the sterilized fluid for infusion into a patient.

### 10 Background of the Invention

Patients undergoing hemofiltration, hemodialysis, hemodiafiltration, ultrafiltration, or other form of renal replacement therapy need replacement fluid, dialysate, or infusate which is free of biological contaminants. Given the large amount of sterile fluid needed by such therapies and the current method of spiking multiple  
15 bags of replacement fluid, dialysate, or infusate, there is a risk of touch contamination resulting in the introduction of biological contaminants into the fluids. Making the appropriate connections, then filtering the fluid greatly reduces this risk to the patient. It would be advantageous if the same equipment used in renal replacement therapy, such as hemofiltration, could be reconfigured for on-line decontamination of  
20 prepackaged solutions such as dialysate to produce the large volumes of sterilized replacement fluid required for the therapy.

Presently methods to produce volumes of dialysate from tap water are known, but require complex water purification / standardization equipment, since impurities and cleaning additives such as chlorine vary greatly in tap water from municipality to municipality and within a municipality over time. (See Twardowski U.S. Patent Nos.  
25 6,146,536 and 6,132,616.)

Moreover, dialysate solution, whether prepared online or prepackaged, while of the proper concentration for use as a sterile replacement fluid, is not deemed to be sufficiently free of pathogenic contaminants to allow the injection of such a fluid into

a patient. In hemodialysis, the dialysate never enters the patient's body, but instead flows past a semipermeable membrane that permits impurities in the blood to osmose through the membrane from the higher concentration blood to the lower concentration dialysate. Thus dialysate, intended for extracorporeal use only, is less expensive than solutions prepared as replacement fluids, which will be injected into a patient.

Attempts to render dialysate sufficiently sterile for use as a replacement fluid in hemofiltration and hemodiafiltration have focused on a continuous sterilization process that requires a separate dialysate filtration / purification apparatus that must be periodically purged and verified to provide sufficient constant flow of sterile replacement fluid required for hemofiltration. (See Chavallet, U.S Patent Nos. 6,039,877 and 5,702,597.) Such devices are necessarily complicated and require separate pumping systems for the sterilization process.

However, if dialysate or other fluid of similar physiological make up could be converted to sterile replacement fluid in the same filter used for hemofiltration or hemodiafiltration, utilizing the same pumps, and without the need for periodic quality-controlled filter purging, a renal replacement therapy unit could be made significantly more simple for reconfiguration to a hemofiltration process to produce low cost sterile replacement fluid in situ. Moreover, the ready availability of pre-connected, disposable filtration and fluid pathway kits that have been sterilized and sealed by the manufacturer would significantly reduce the opportunity for touch contamination during the preparation of sterile replacement fluid.

#### Summary of the Invention

The present invention provides devices and methods for producing sterile replacement fluid in a unit that is subsequently used for renal replacement therapy on a patient. The system can be used both to sterilize non-sterile fluid and to sterilize sterile fluid contaminated (e.g., by touch contamination) during connection due to improper technique. In a first embodiment, a system is provided to perform a method that includes the steps of providing a renal replacement therapy unit that has a filter with a membrane separating a waste side of the filter from a clean side. The membrane has a pore size smaller than the non-sterile and pyrogenic material to be

filtered. The renal replacement therapy unit also includes a first container of a solution of suitable concentration for use as a replacement fluid that may include the non-sterile and/or pyrogenic material, or sterile fluid contaminated (e.g., by touch contamination) during connection due to improper technique. The first container is in fluid communication with the waste side of the filter. The unit also includes a second container that is adapted to hold sterile replacement fluid. The second container is in fluid communication with the clean side of the filter. A pump, generally the ultrafiltrate pump, is in fluid communication with the first container and the second container. The pump is capable of switching between a first direction that pumps fluid out of the first container and a second direction that removes waste from the blood through the filter. A second pump, called a replacement fluid pump, pumps fluid out of the second container. The method further includes the step of running the pump in the first (reverse) direction to pump the solution of suitable concentration from the first container into the waste side of the filter. The solution from the first container is filtered through the membrane of the filter to trap the non-sterile and pyrogenic material on the waste side of the filter and produce sterile replacement fluid in the clean side of the filter. The sterile replacement fluid that flows from the clean side of the filter is collected in the second container. During therapy the pump switches to run in the second (forward) direction to pump waste from the blood through the filter. The sterile replacement fluid is pumped from the second container into the blood by a second pump. The sterile replacement fluid is used to perform renal replacement therapy on a patient.

Another embodiment is a pre-connected, sterilized fluid management kit for use in presterilizing replacement fluids prior to renal replacement therapy. The kit includes various disposable components of a renal replacement therapy unit. In one embodiment, the kit includes a fluid pumping and balancing system, one or more sterile fluid reservoir, a plurality of tubes conventionally used in a renal replacement therapy, a waste line, and one or more replacement fluid container. Each of the plurality of tubes has a first end in fluid communication with the fluid pumping and balancing system and a second end coupled, in some cases releasably coupled to and

in fluid communication with the sterile fluid reservoir. The replacement fluid container tube has a first end coupled to the fluid pumping and balancing system and a second end coupled or adapted to couple to a replacement fluid container. The kit is sterilized and packaged in a container at the time of manufacturing to prevent contamination prior to use in a renal replacement therapy unit.

Another embodiment is a system for batch sterilization of replacement fluid and renal replacement therapy using the sterilized fluid. The system includes a renal replacement therapy unit adapted to releasably receive a sterilized kit and a sterilized kit having preconnected disposable elements of the renal replacement therapy unit.

The kit includes a fluid pumping and balancing system, which may in certain cases take the form of a removable cartridge, a plurality of connectors, each having a first end coupled to the fluid pumping and balancing system and a second end adapted to couple, in some cases releasably couple, to the renal replacement therapy unit (for example, a hemofiltration machine), a sterile replacement fluid container coupled, in some cases releasably coupled to the fluid pumping and balancing system through a plurality of tubes, and a tube having a first end coupled to the fluid pumping and balancing system and a second end adapted to couple, in some cases releasably couple to a container of solution to be sterilized.

Another embodiment is a method for producing sterile replacement fluid in a renal replacement therapy unit. The method includes the steps of providing a renal replacement therapy unit, a sterilized kit that includes certain disposable elements of the unit, and a container of solution of suitable concentration for use as a replacement fluid. The unit is adapted to releasably receive the sterilized kit. The kit includes a plurality of tubes adapted to releasably couple to the renal replacement therapy unit, a preconnected or connectable sterile replacement fluid container and a tube having an end adapted to couple, in some cases releasably couple to the solution container. The method further includes the steps of releasably coupling the sterilized kit to the renal replacement therapy unit, coupling (in some cases releasably coupling) the tube to the container of a solution of suitable concentration for use as a replacement fluid, pumping the solution through the renal replacement therapy unit to sterilize it, and

capturing the sterilized solution in the sterile replacement fluid container for use in renal replacement therapy.

#### Brief Description of the Drawings

Fig. 1 depicts an embodiment of a hemofiltration unit performing the therapy.

5 Fig. 2A is a schematic of the embodiment of FIG. 1, performing hemofiltration therapy.

Fig. 2B is a schematic of the embodiment of FIG. 3 performing solution sterilization.

10 Fig. 3 is an embodiment of a hemofiltration unit operating in the reverse pumping mode used for solution sterilization

Fig. 3A depicts an embodiment of a hemofiltration unit used to mix dialysate.

Fig. 4 is another embodiment of a disposable unit adapted to couple to a hemofiltration unit for solution sterilization, priming, and subsequent hemofiltration therapy.

15 Fig. 5 is an embodiment of a hemofiltration unit performing solution sterilization demonstrating the fluid flow paths.

Fig. 6 is an embodiment of a hemofiltration unit in priming mode.

20 Fig. 7A is an embodiment of a renal replacement therapy system (without tubing and without filter) showing the installation of a fluid management kit in a hemofiltration unit adapted to receive the kit.

Fig. 7B shows the embodiment of the system of Fig. 7A with the kit fully installed (without tubing and without filter).

#### Detailed Description

25 A hemofiltration device 1 is depicted in Fig. 1. In a conventional forward pumping hemofiltration mode, a draw blood line 20 carries blood, for example arterial blood, from the patient 92 to a filter 30. A membrane in the filter 30 allows waste products such as urea and other undesirable metabolic byproducts that are blood contaminants together with water to pass through the filter membrane to the waste side of the filter 30 and out a side port 40 into a waste line 50. The waste line 50

drains the waste filtrate 61 into a waste container 60. The filter membrane does not permit blood cells and higher molecular weight proteins to pass through with the waste filtrate and thus concentrated, purified blood passes out the filter top port 70. The fluid volume lost as waste filtrate during the hemofiltration process must now be

5 replaced in the concentrated, purified blood to return the blood to its proper physiologic concentration. Accordingly, a measured volume of sterile replacement fluid 81 from a sterile fluid reservoir 80 is added to the filtered blood in an amount equal to the volume of waste filtrate removed during the hemofiltration process. A fluid balancing system (not shown in FIG.1) that measures the waste filtrate removed

10 and then dispenses the proper volume of replacement fluid needed is located inside the hemofiltration unit 1. Systems and devices for fluid balancing have been described in U.S. Patent Application 09/513,773, filed February 25, 2000, the contents of which are incorporated herein in their entirety by reference. The replacement fluid flows from the replacement sterile fluid reservoir 80, through the replacement fluid line 10,

15 to the balancing system in the hemofiltration unit 1. The reconstituted blood, now consisting of the concentrated, purified blood and the measured amount of replacement fluid, is returned via the return blood line 90, for instance a venous line, to the patient 92.

FIG. 2A shows a schematic representation of the hemofiltration process. A

20 draw blood line 20 carries blood from the patient to the filter 30. The blood pump 25 pushes the blood through the filter, and the pressure differential due to the positive pressure of the blood drives the blood across the membrane. A balancing system 48 meters the waste or blood, water, and contaminants through the membrane 35 of the filter 30, metering out the water and contaminants into the waste side 33 of the filter

25 and allowing concentrated purified blood to pass out the clean side 37 of the filter and into the filter top port. 70. The waste filtrate exits the waste port 40 of the filter 30 and passes into the balancing system 48. Sterile replacement fluid flows from the sterile replacement fluid reservoir 80 through the replacement fluid line 10 to the balancing system 48 where a measured amount of sterile replacement fluid equal to the amount

30 of waste filtrate passed through the balancing system 48 is allowed to combine with



the concentrated blood in the return line 90 and return to the patient. The waste filtrate that has passed through the balancing system passes through the waste line 50 and into the waste container 60.

If the therapy requires hemofiltration and ultrafiltration, then an ultrafiltration pump 45 removes excess fluid from the patient's blood and dumps the excess fluid into the waste container 60. This excess fluid removed by the ultrafiltration pump 45 does not pass through the balancing system and thus is not matched by an equal amount of replacement fluid. The system may use additional pumps such as a waste pump and a replacement fluid pump as part of the fluid balancing system to assist the proper fluid flow through the system.

FIG. 3 shows an embodiment of the present invention prior to connection to the patient 92 to perform therapy. The hemofiltration unit 1 is configured to convert a solution of suitable electrolyte concentration for use as a replacement fluid 82, for example dialysate, in a container 62 to sterile replacement fluid 81 that is pumped to a container adapted to hold the sterile fluid, such as a sterile fluid reservoir 80, via a filtration sterilization process. While the solution 82 to be converted will have the proper electrolyte concentration required of replacement fluids, there is a concern that the solution will include non-sterile and/or pyrogenic material, for example pathogens such as bacteria, and thus not be sufficiently sterile to be injected into a patient as a replacement fluid. Thus, the hemofiltration unit can be used to filter the solution to remove bacteria and other pathogens and to prepare sterile replacement fluid for a subsequent hemofiltration procedure by running the appropriate pump in the hemofiltration unit in reverse of the pumping mode used for conventional hemofiltration. In a preferred embodiment, the hemofiltration unit is adapted to receive certain disposable components including a fluid pumping and balancing system as more fully explained herein.

FIG. 2B shows the fluid sterilization process schematically. A pump in fluid communication with the fluid container 62, for instance an ultrafiltration pump 45, is run in reverse of the direction that the pump is conventionally run during ultrafiltration therapy to draw fluid from the container 62 up through the waste line 50

and into the waste side 33 of the filter 30 via the waste port 40. The pump 45 forces the fluid through the filter membrane 35 into the clean side 37 of the filter. Because the non-sterile material in the fluid, for instance bacteria or pyrogen, is larger than the pore size of the filter membrane 35, bacteria in the fluid remain on the waste side 33 of the filter. The filtered fluid, now rendered sterile, emerges as sterile replacement fluid from the top port 70 of the filter and flows through the return blood line 90 into the sterile replacement fluid reservoir 80.

In other methods, the hemofiltration unit is configured to mix certain solutions 82 and 83, such as saline and concentrate, sterilize the mixture and convert it into a suitable electrolyte concentration for use as a sterile replacement fluid 81, as shown in Fig. 3A. A first container 82 of concentrated electrolytes, e.g., any one or more of sodium lactate, potassium, calcium, magnesium chloride, sodium chloride, bicarbonate, and/or other appropriate salts, and/or other elements, is connected to a Y-connector 84. A second container 83 of water, ringers lactate, saline, or other like solution is also connected to Y-connector 84. The two solutions are then mixed as they pass through Y-connector 84 and then pass through filter 70. The mixed and filtered fluid, now rendered sterile, emerges as a sterile replacement fluid from the top port 70 of the filter and flows through the return blood line 90 into sterile replacement fluid reservoir 80.

The hemofiltration unit automatically primes the remainder of the fluid pathway when all of the replacement fluid is transformed into sterile replacement fluid. The priming process is described more fully herein.

Once the fluid pathway is primed, the hemofiltration unit is ready to be connected to the patient for renal replacement therapy. Referring again to FIGS. 1 and 2A, the blood pump 25 pumps the patient's blood through the filter 30, the balancing system 48 meters fluid from the sterile fluid reservoir 80, and the trapped bacteria on the waste side 33 of the filter pass into the container 60 along with waste blood water. In a preferred embodiment, the now-empty container 60 previously containing the solution 82 can now be used as a waste container for the hemofiltration therapy. A system using more than one filter can also be employed. Further, the system can be

used to mix a concentrate solution with another solution, as described in the above-described method and Fig. 3A.

While the embodiments shown are described for hemofiltration therapy, the devices and methods can be used for blood processing, infusive therapies, or any renal replacement therapy, for instance hemodiafiltration, and can also be used for hemodialysis. Moreover, while the hemofiltration unit described is a volumetric system, this method can be readily employed with a mass-metric hemofiltration system that uses scales instead of balance chambers or flow meters to balance flows.

In a preferred embodiment, the fluid pumping and balancing system and optionally other elements may be preconnected, prepackaged, sterilized and sealed by the manufacturer into a disposable unit such as a kit to reduce touch contamination that can be introduced during set-up of the fluid sterilization process. A renal therapy unit is adapted to receive the kit, which is releasably coupled to the unit, to form a system for batch sterilization of replacement fluid and subsequent renal replacement therapy using the sterilized fluid. Following therapy, the kit may be removed and discarded and a new kit can be installed for a subsequent fluid sterilization and therapy procedure.

FIG. 4 shows an embodiment of a pre-connected, disposable fluid management kit 100. The embodiment includes a filter 300, for example a hemofilter, and a sterile fluid reservoir 800 connected to a fluid pumping and balancing system 12 through various tubes or lines 900, 10, 200. A first end 901, 101, 201 of each tube 900, 10, 200 is coupled to the fluid pumping and balancing system 12 and a second end 902, 102, 202 of each tube 900, 10, 200 is releasably coupled to the sterile fluid reservoir 800 via connectors 93, 11, 21. Manual clamps 94 may also be used to control fluid flow when disconnecting lines. A waste line 500 has a first end 501 coupled to the fluid pumping and balancing system 12 and a second end 502 removably sealed by a cap 52. In the embodiment of FIG. 4, the fluid management kit includes a filter 300 in fluid communication with the pumping and balancing system 12. The pre-coupled, disposable components of the fluid management kit are sterilized by the manufacturer and sealed in a suitable container 130 to guard against

contamination. The container 130 may be a poly bag, Tyvek®, paper or other suitable material. The sterilization process used by the manufacturer may be of any conventional method used for sterilizing medical equipment such as gamma irradiation, chemical sterilant such as ethylene oxide, steam, e-beam or the like. The fluid pumping and balancing system 12 of the embodiment of FIG. 4 includes a blood pump 250, an ultrafiltrate pump 450, a fluid balancing system 480, and a venous air detector 515. The fluid balancing system 480 illustrated in the embodiment is a volumetric system, however it could also be gravimetric flow meters or other means of fluid balancing. The components of the fluid management kit may be connected to form a fluid pathway in any conventional structure used for hemofiltration and ultrafiltration such as the structures shown in the embodiments of FIGS. 1–3. Similarly, the hemofiltration filter 300 may be integrated into the fluid pathway in any conventional structure. In certain embodiment, the hemofiltration filter is not part of the disposable kit.

In the embodiment of FIG. 4, the sterile fluid reservoir 800 is releasably coupled to the fluid pumping and balancing system 12 through a blood return line 900, a sterile replacement fluid line 10 and a draw blood line 200 through connectors 93, 11, and 21. The connectors 93, 11, and 21 can be Luer connectors, proprietary connectors or any other connectors that will provide a hermetic seal that can be decoupled by a user. The sterile fluid reservoir 800 may be of any size required by the therapy, but preferably between 1 and 75 liters and most preferably between 5 and 50 liters, generally approximately 20 liters. The waste line 500 can later be used as a waste line during hemofiltration.

Use of the pre-packaged, sterilized fluid management kit greatly reduces the risk of touch contamination. For instance, in the embodiment of FIG. 4, the only connection that must be made by the user during set up is the connection of the replacement fluid container to the waste line 500. Replacement fluid is commonly provided in one-liter bags, thus requiring up to 50 or more connections to sterilize a sufficient amount of fluid depending on the prescribed therapy. In the embodiment of FIG. 4, all of these connections are made on the waste side of the filter, and

accordingly any contamination introduced by the connection procedure is filtered out as the solution moves through the system to the sterile fluid reservoir 800 during batch sterilization.

FIG. 5 shows a schematic of the fluid flow of the fluid management kit 100 of the embodiment of FIG. 4 in use in a system for batch sterilization of replacement fluid and subsequent renal replacement therapy, where the system includes the hemofiltration unit fitted with a disposable fluid management kit. The system is best seen in FIGS. 7A and 7B, where the system 1000 for batch sterilization of replacement fluid and renal replacement therapy using the sterilized fluid includes a renal replacement therapy unit 1100 adapted to releasably receive a sterilized fluid management kit and a sterile fluid management kit 1200 (tubing, bags, and filter not shown). FIG. 7A shows the installation of the kit 1200 into the unit 1100. Returning now to FIG. 5, the fluid flow illustrates the batch sterilization process. The second end 502 of the waste line 500 has been releasably coupled to the replacement fluid containers 600. All of the other fluid connectors 93, 11, 21 have been preconnected by the manufacturer and thus are not a source of touch contamination during set-up. Only one pump 450 runs during sterile filtration. All other pumps and the balancing system are dormant during sterile filtration. Sterile filtration continues until the entire batch has been processed.

During replacement fluid sterilization, the pump 450, which in this embodiment is the ultrafiltration pump, runs in reverse (a second direction) of its conventional therapeutic pumping direction (a first direction) through filter 300 until the containers 600 of replacement fluid are empty. The emptying of the container results in air pumped into the filter, which is sensed by the venous air detector 515, best seen in FIG. 4. When the venous air detector 515 senses the presence of air, software in the hemofiltration system triggers the pump 450 to reverse the pumping direction to the first direction and to prime the system including the filter. This first direction pumps fluid from the sterile fluid replacement reservoir 800. This priming process is shown in FIG. 6. Since the blood return line 900, the draw line 200 and the replacement fluid line 10 are all connected to the sterile replacement fluid

reservoir 800, fluid can be drawn out and air pushed into the reservoir 800 where it floats out of solution. The pump 450 rotates in the forward, or first, pumping direction, metering fluid from the bag 800 and forcing air into the bag 800 from the return line 900. Fluid is drawn through the replacement fluid line 10 and into the  
5 fluid balancing system 480 forcing air out into the venous return line 900. Sterile replacement fluid is pushed back across the filter 300 priming the waste side of the filter and dumping air into the former replacement fluid containers, now the waste containers 570. Because the reservoir 800 of sterile replacement fluid acts as a bubble trap, the hemofiltration system, exclusive of the bag, is primed and free of air.

10 An integrity test can be performed on the filter to verify that the replacement fluid was properly filtered during sterilization. The test may, for example, be substantially similar to that used in manufacture of the filter itself, and measures the partial pressure of the wet filter using the air from the arterial line as the test medium. The replication of the manufacturer's test assures that the filter is leak free and thus  
15 the filtered fluid is sterile and safe to use as a replacement fluid. Another example of an integrity test may be measuring pressure drops through the filter using fluid and no air.

In certain embodiments, a blood leak detector 516 can be incorporated into the fluid pumping and balancing system and used as a redundant test of filter integrity. If  
20 the filter demonstrates a leak after the patient has been connected, the blood leak detector will alarm.

Once a test of filter integrity is successfully performed and the system has been primed as previously described, the unit is ready for renal replacement therapy, for instance hemofiltration or hemodiafiltration. The second end of each of the draw  
25 and return lines is decoupled from the sterile replacement fluid reservoir and each is releasably coupled to the appropriate vascular access of the patient and renal replacement therapy is initiated. The vascular access can be a native fistula, a synthetic graft, a catheter a subcutaneous port or other conventionally used method.

Although the foregoing invention has, for the purposes of clarity and  
30 understanding, been described in some detail by way of illustration and example, it

will be obvious that certain changes and modifications may be practiced that will still fall within the scope of the appended claims. For example, the devices and methods of each embodiment can be combined with or used in any of the other embodiments.

What is claimed is:

1. A method for producing sterile replacement fluid in a renal replacement therapy unit, the method comprising the steps of:

5 providing a renal replacement therapy unit having a filter with a membrane having a pore size smaller than a non-sterile material, the membrane separating a waste side from a clean side of the filter; a first container of a solution, the first container in fluid communication with the waste side of the filter; and a second container adapted to hold sterile replacement fluid, the second container in fluid communication with the clean side of the filter;

10 pumping the solution from the first container into the waste side of the filter;

filtering the solution from the first container through the membrane of the filter to trap the non-sterile material on the waste side of the filter and produce sterile replacement fluid in the clean side of the filter; and

15 collecting the sterile replacement fluid that flows from the clean side of the filter in the second container for use in renal replacement therapy.

2. The method of claim 1, wherein the renal replacement therapy unit further comprises a reversible pump.

20 3. The method of claim 1, wherein the solution is dialysate solution.

4. The method of claim 1, wherein the solution in the first container is selected from the group consisting of water, ringers lactate, or saline, and wherein the unit further comprises a second container of a concentrated electrolyte solution, the second container in fluid communication with the first container and the waste side of the filter.

25



5. The method of claim 1, wherein the solution in the first container mixes with the solution in the second container as the solution in the first container and the solution in the second container pass through the filter to produce a resulting solution of suitable electrolyte concentration.
- 5                    6. The method of claim 1, wherein replacement fluid is sterile infusate.
7. The method of claim 1, wherein the renal replacement therapy is hemofiltration.
8. The method of claim 1, wherein the renal replacement therapy is hemodiafiltration.
- 10
9. The method of claim 1, wherein the renal replacement therapy is hemodialysis.
10. The method of claim 1, wherein following the step of switching, the method further comprises the step of expelling the non-sterile material and waste into the first container.
- 15
11. The method of claim 1, wherein the entire content of the first container is sterilized through the filter membrane before initiating renal replacement therapy.
12. The method of claim 11, wherein following initiating renal replacement therapy, the substantially empty first container that previously held the solution of suitable concentration for use as a replacement fluid is now used as a waste container, the method further comprising the step of expelling waste material
- 20

from the waste side of the filter into the waste container during renal replacement therapy.

13. The method of claim 11, wherein the renal replacement therapy unit further comprises a venous air detector in fluid communication with the first  
5 container and the second container, the method further comprising the step of sensing air with the venous air detector upon the sterilization of the entire contents of the first container.

14. The method of claim 13, wherein the step of sensing air occurs prior to the step of initiating renal replacement therapy.

10 15. The method of claim 14, wherein prior to the step of initiating renal replacement therapy, the method further comprises the step of triggering the initiation of renal replacement therapy when the venous air detector senses air.

16. The method of claim 15, further comprising the step of  
15 priming the renal replacement unit after the step of initiating renal replacement therapy.

17. The method of claim 1, the method further comprising the step of verifying the integrity of the filter.

18. The method of claim 17, further comprising the step of  
20 verifying the integrity of the filter by measuring the partial pressure of the wet filter using the air as a test medium.

19. The method of claim 1, wherein the renal replacement therapy unit further comprises a blood leak detector, the method further comprising the step of causing the blood leak detector to alarm if a leak is detected in the filter.

20. The method of claim 1, wherein following the step of initiating renal replacement therapy, the method further comprises the step of injecting the sterile replacement fluid into a patient via the blood return line.

21. A pre-connected, sterilized fluid management kit for use in sterilizing replacement fluids for use in renal replacement therapy, the kit comprising:

- a fluid pumping and balancing system;
- a sterile fluid reservoir;
- a plurality of tubes conventionally used in a renal replacement therapy, each tube having a first end in fluid communication with the fluid pumping and balancing system and a second end coupled to and in fluid communication with the sterile fluid reservoir; and
- a waste tube having a first end coupled to the fluid pumping and balancing system and a second end adapted to couple to a replacement fluid container before sterile filtration,

wherein the kit is sterilized and packaged in a container to prevent contamination prior to use in a renal replacement therapy unit.

22. The kit of claim 21, further comprising a filter in fluid communication with the fluid pumping and balancing system.

23. The kit of claim 21, wherein a first one of the plurality of tubes is a blood draw line.

24. The kit of claim 23, wherein a second one of the plurality of tubes is a blood return line.

25. The kit of claim 21, wherein the coupling is a releasable coupling.

26. The kit of claim 24, wherein a third one of the plurality of tubes is a replacement fluid line.

5                    27. The kit of claim 26, wherein a fourth one of the plurality of tubes is a waste line.

28. The kit of claim 21, further including a connector, and wherein a second end of at least one of the plurality of tubes is releasably connected to the sterile replacement fluid reservoir by the connector.

10                   29. The kit of claim 28, wherein the connector is adapted to releasably couple to a vascular access device.

30. The kit of claim 28, wherein the connector is a Luer connector.

31. The kit of claim 21, further including a sterilized cap, and wherein the sterilized cap removably seals the second end of the waste line.

32. A method for producing sterile replacement fluid in a renal replacement therapy unit, the method comprising the steps of:

- 5 providing a renal replacement therapy unit adapted to releasably receive a sterilized fluid management kit, the kit including pre-connected disposable elements of a renal replacement therapy system; a sterilized fluid management kit  
having disposable elements of a renal replacement therapy system including a plurality of tubes adapted to releasably couple to the renal replacement therapy unit, a sterile replacement fluid reservoir and a tube having an end adapted to releasably couple to a solution container; and a container of a solution of suitable concentration  
10 for use as a replacement fluid;  
releasably coupling the sterilized fluid management kit to the renal replacement therapy unit, forming the renal replacement therapy system;  
releasably coupling the tube to one or more container of one or more solution of suitable concentration for use as a replacement fluid;  
15 pumping the solution of suitable concentration for use as a replacement fluid through the renal replacement therapy system to sterilize the solution; and  
capturing the sterilized solution in the sterile replacement fluid reservoir for use in renal replacement therapy.

33. The method of claim 32, wherein the kit includes a filter.

20 34. The method of claim 32, wherein the container of solution of suitable concentration for use as a replacement fluid is a first container, the method further comprising the steps of:

- decoupling the first container from the tube;  
releasably coupling a second container of solution of suitable  
25 concentration for use as a replacement fluid to the tube;  
pumping the solution from the second container through the renal replacement therapy system to sterilize the solution; and  
capturing the sterilized solution in the sterile replacement fluid reservoir for use in renal replacement therapy.

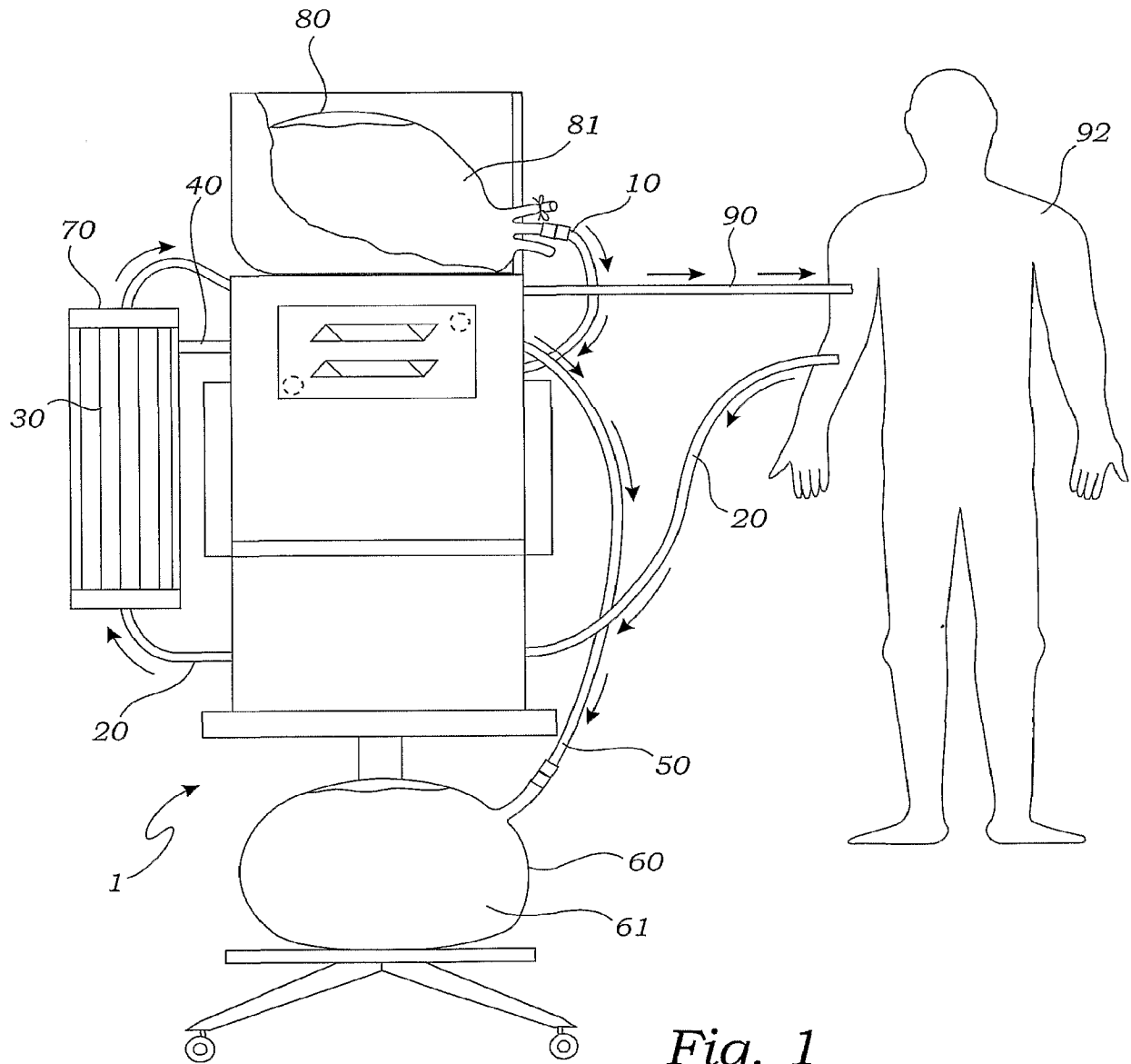
35. The method of claim 32, further comprising the step of decoupling the kit from the renal replacement therapy unit and the container.

36. The method of claim 32, wherein the kit is a first kit, the method further comprising the step of releasably coupling a second kit to the renal replacement therapy unit.

37. A system for batch sterilization of replacement fluid and renal replacement therapy using the sterilized fluid, the system comprising:  
a renal replacement therapy unit adapted to releasably receive a sterilized fluid management kit including pre-connected disposable elements of the system; and  
a sterilized fluid management kit comprising:  
a fluid balancing and pumping system;  
a plurality of connectors coupled at a first end to the fluid balancing and pumping system;  
a sterile replacement fluid container releasably coupled to the fluid balancing and pumping system; and  
a tube having a first end coupled to the fluid balancing and pumping system and a second end adapted to releasably couple to a container of solution to be sterilized.

38. The system of claim 37, wherein at least one of the plurality of tubes releasably coupled to the sterile replacement fluid reservoir is adapted to be decoupled from the reservoir and coupled to a vascular access port in a patient.

1/9



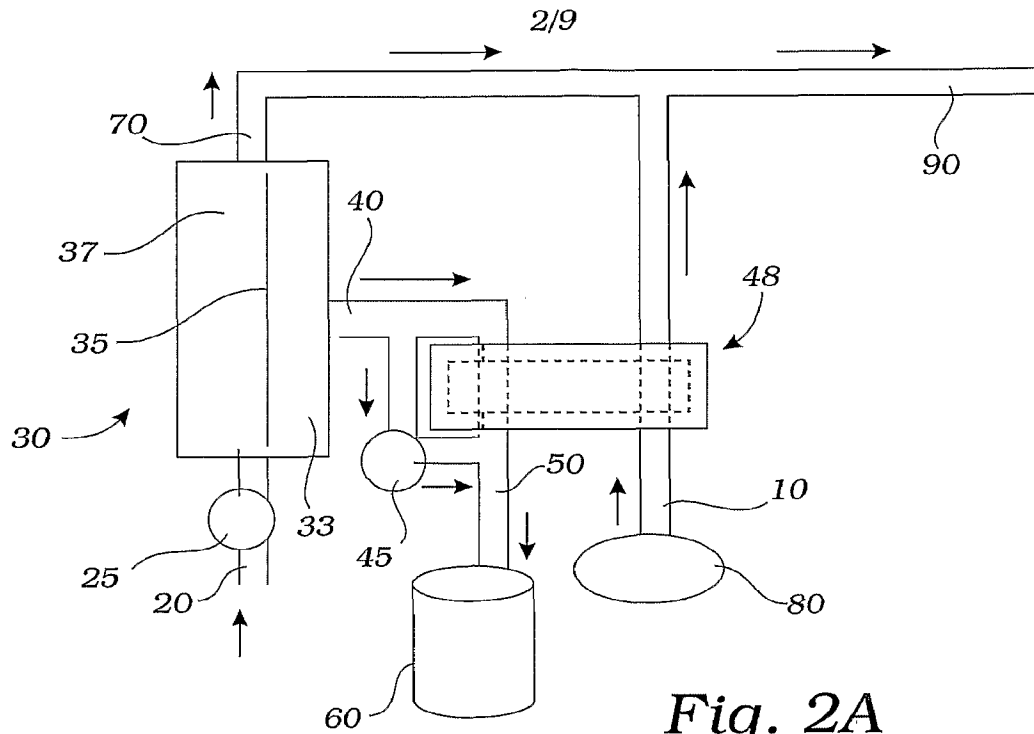


Fig. 2A

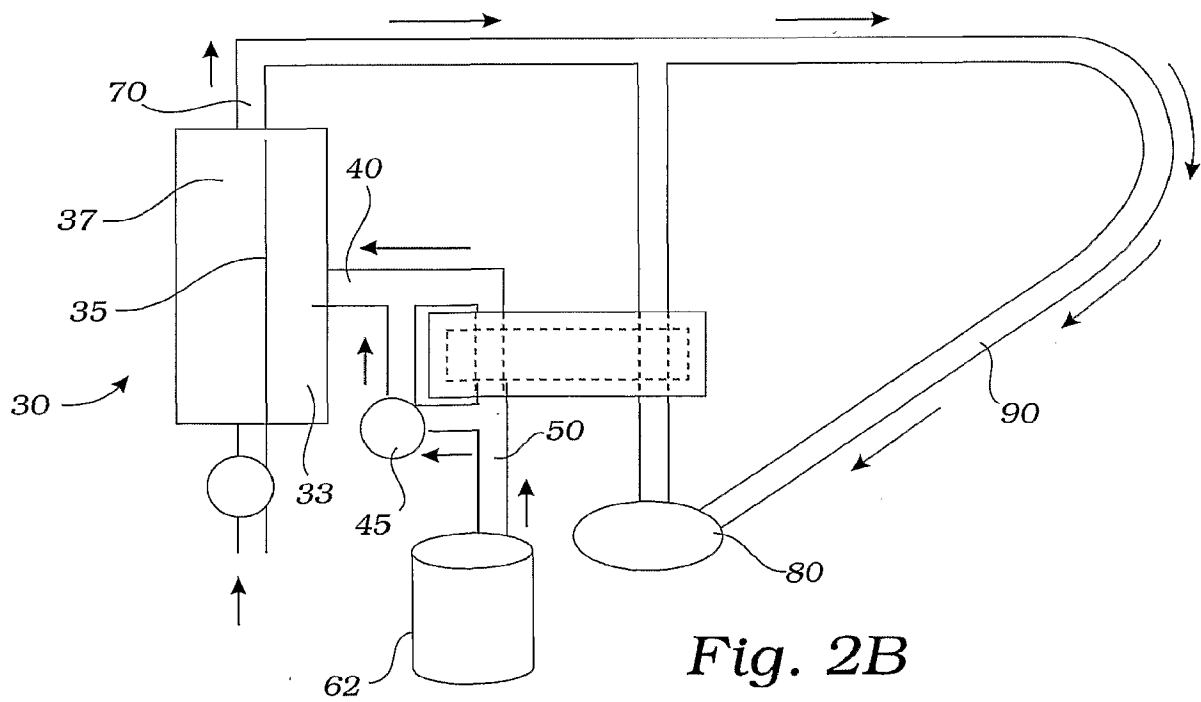
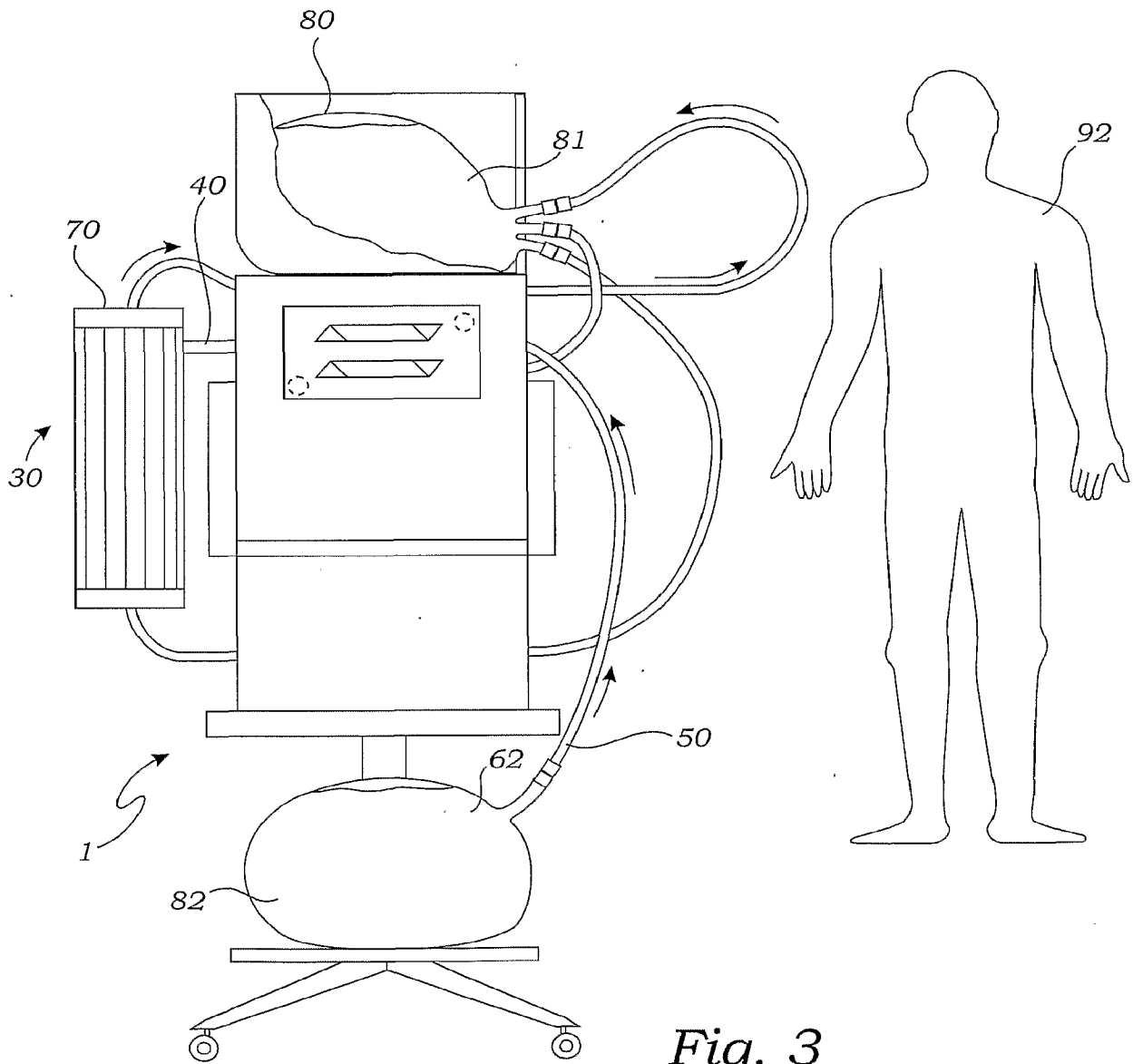
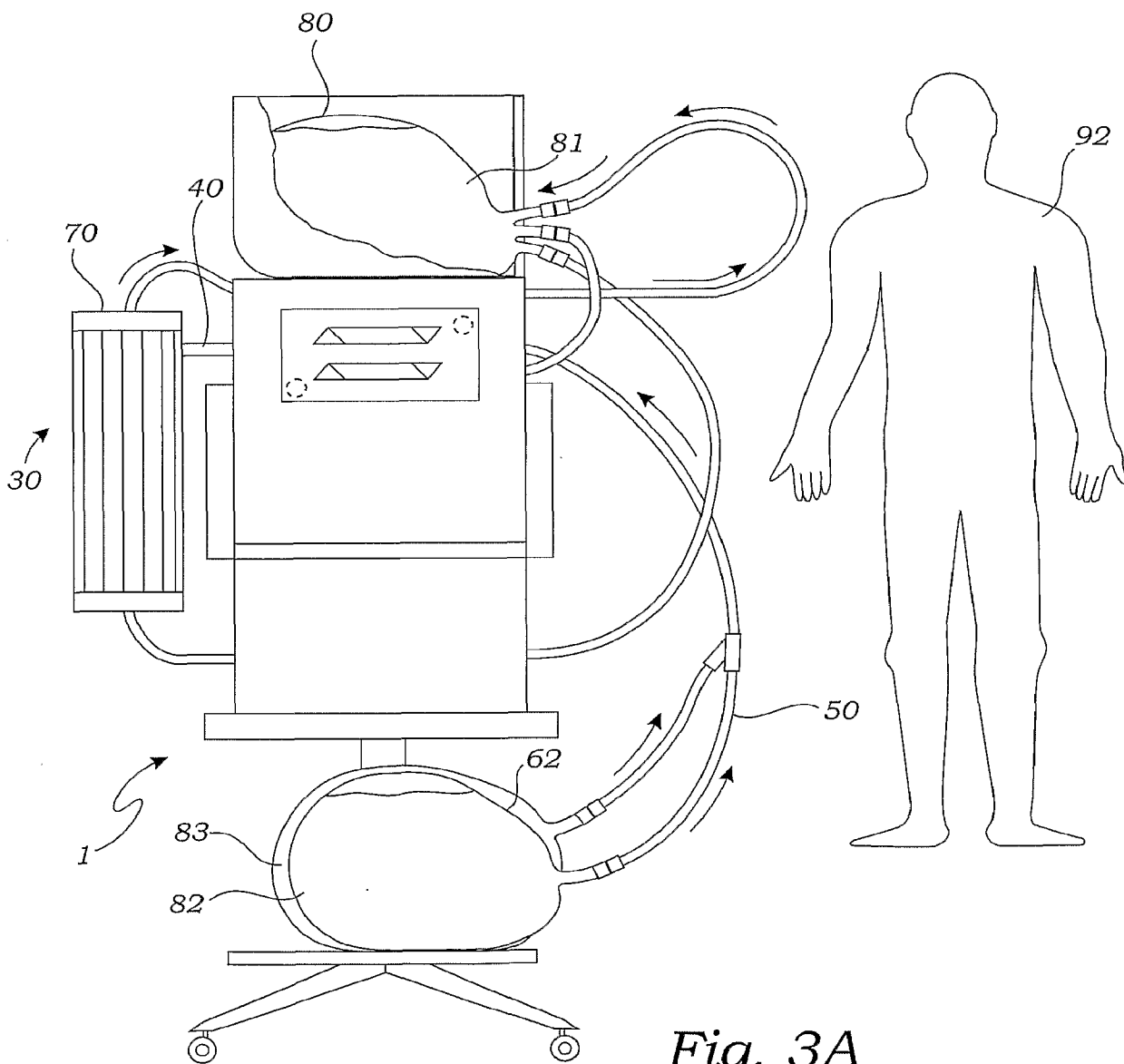


Fig. 2B



3/9

*Fig. 3*



*Fig. 3A*

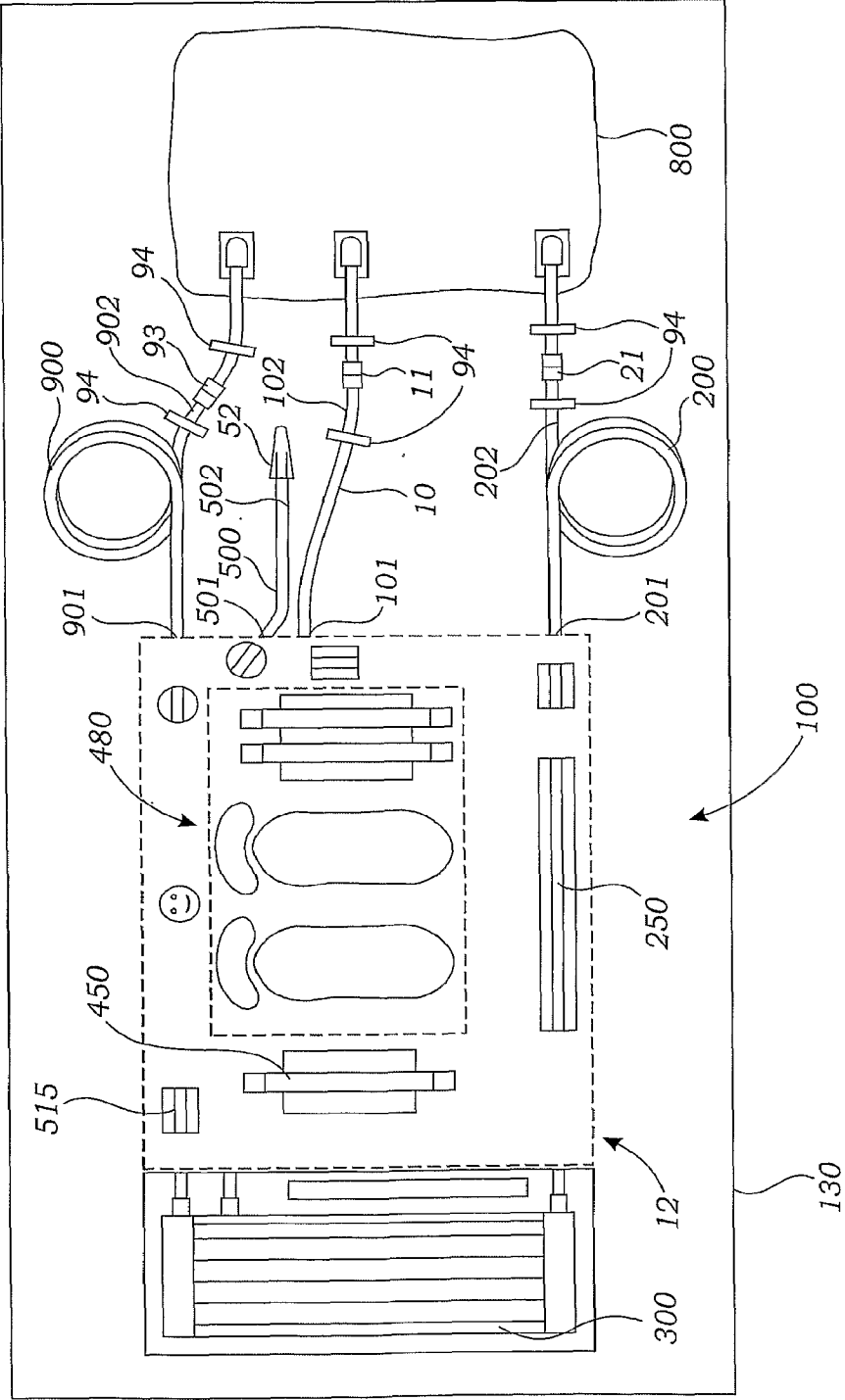


Fig. 4

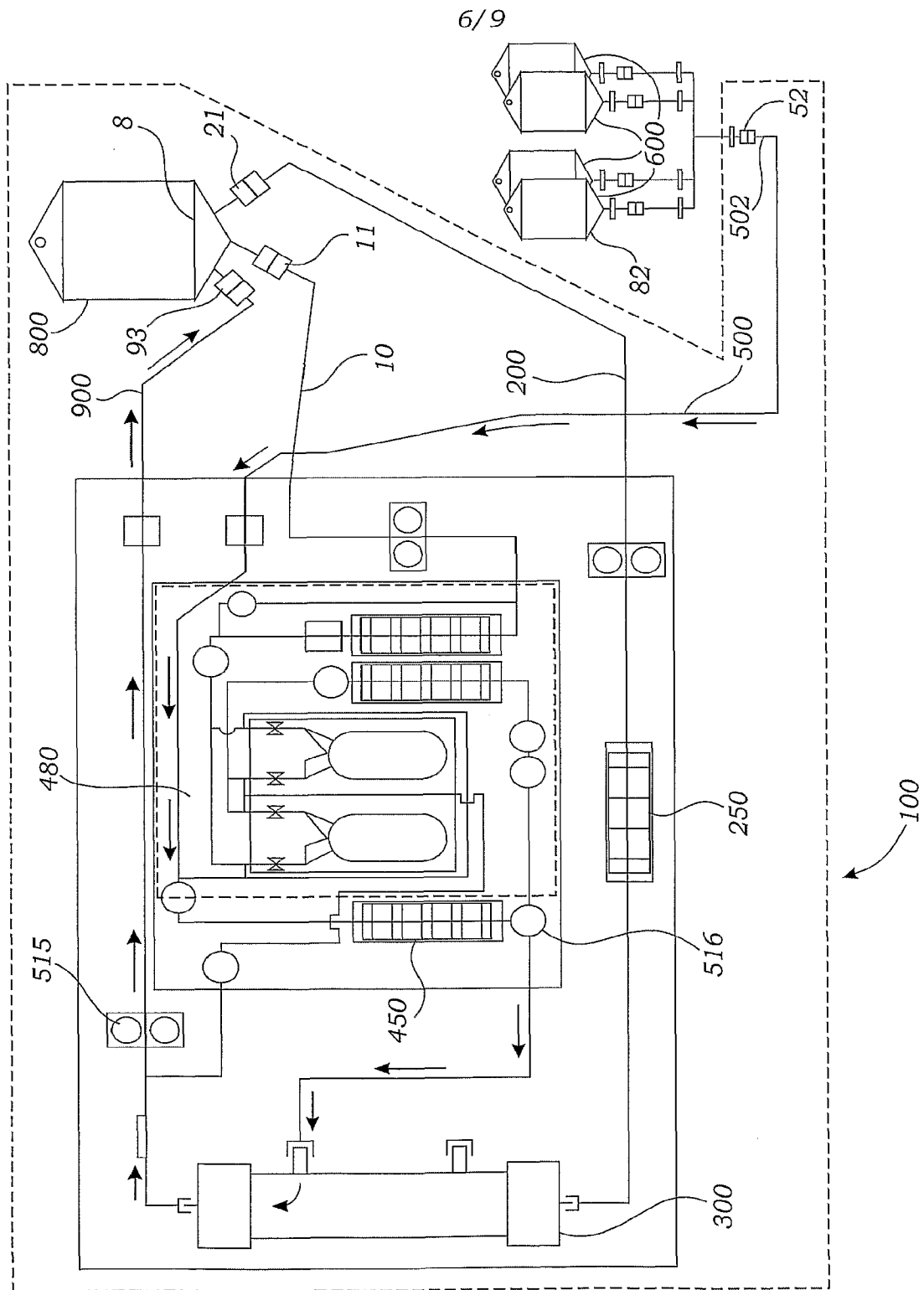


Fig. 5

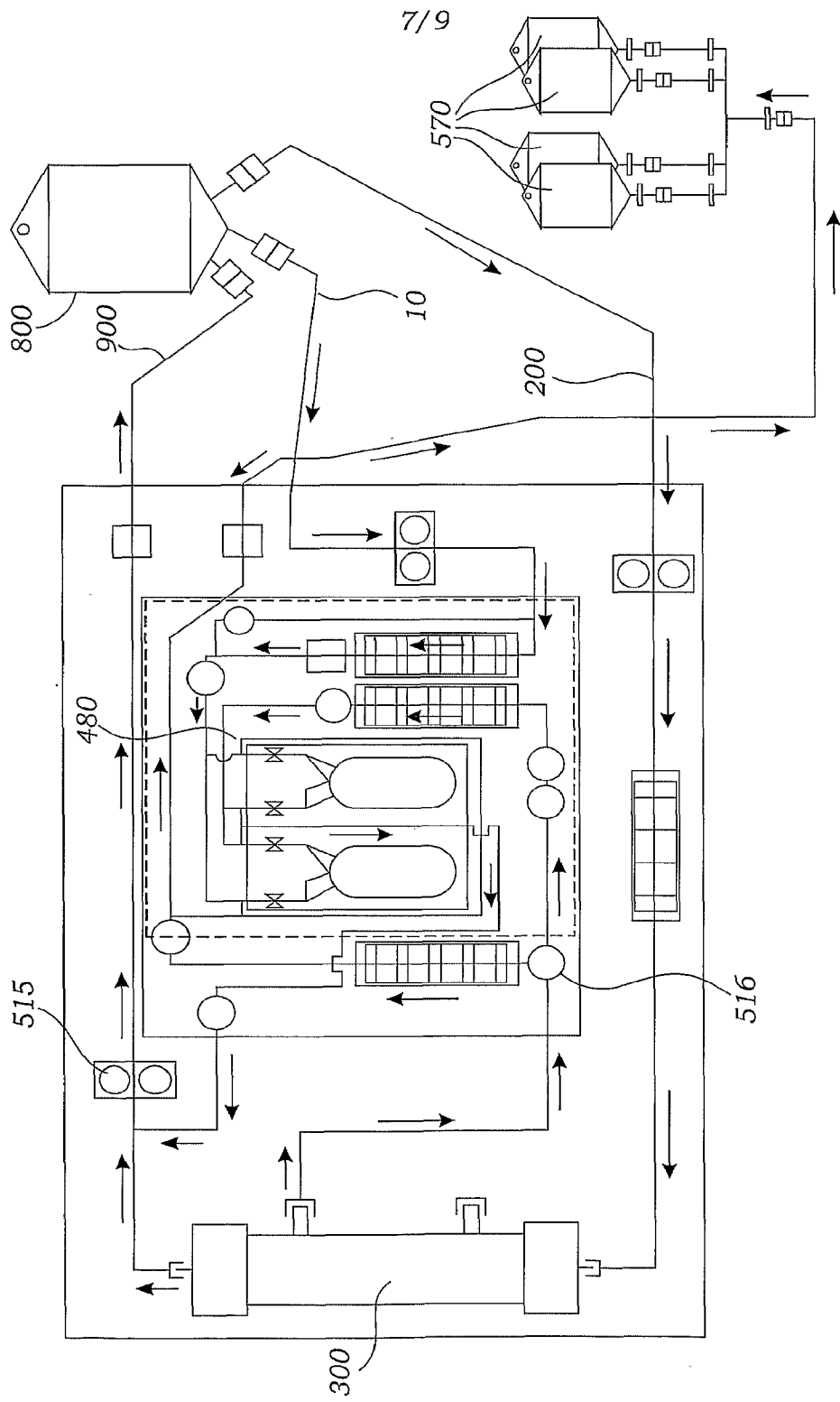
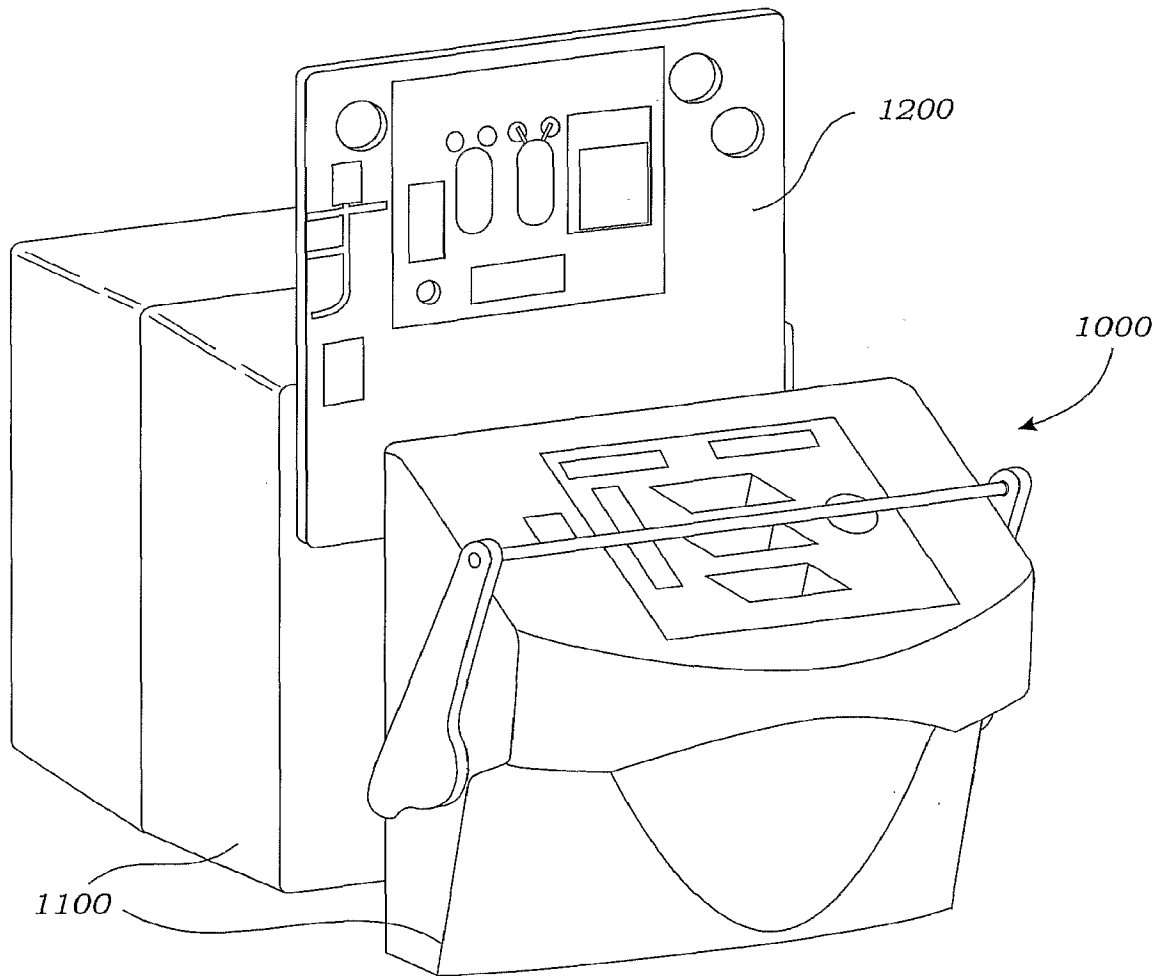
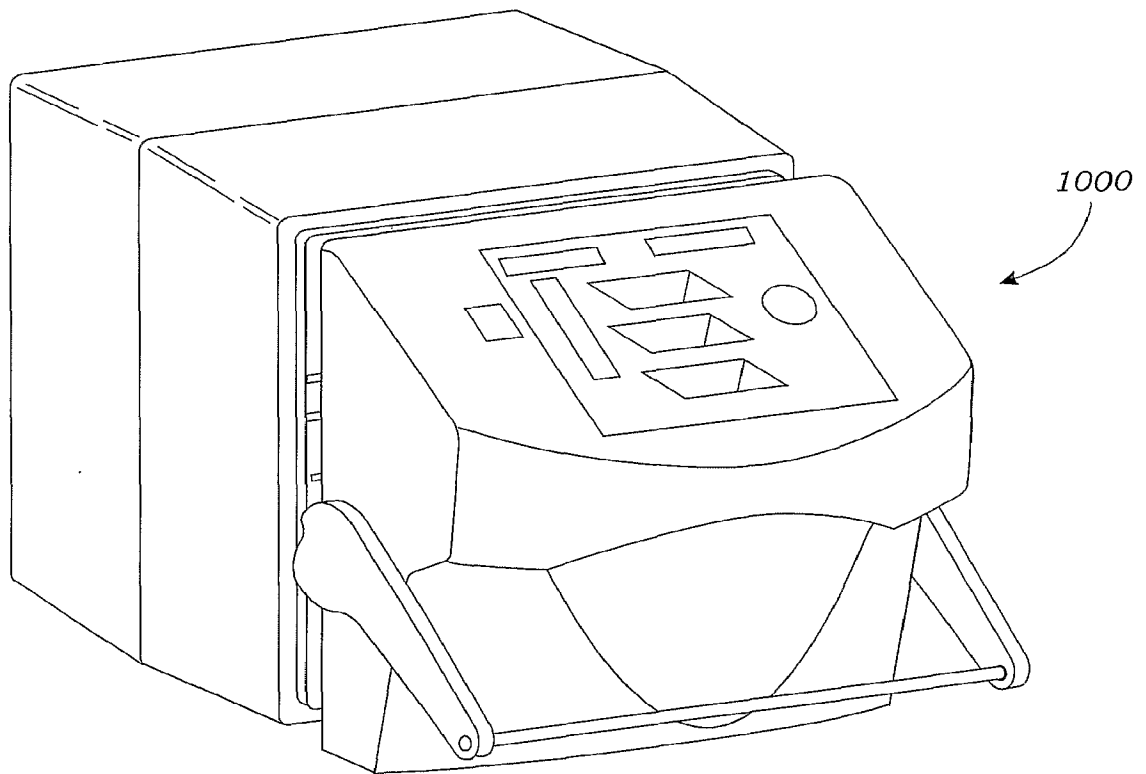


Fig. 6

8/9

*Fig. 7A*



*Fig. 7B*

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/22184

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61M 37/00, 36/00; B01D 61/00, 61/20, 61/30

US CL : 210/85, 103, 106, 195.1, 195.2, 252, 257.1, 257.2, 258, 321.6, 645, 646, 650, 739, 767, 805

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 210/85, 103, 106, 195.1, 195.2, 252, 257.1, 257.2, 258, 321.6, 645, 646, 650, 739, 767, 805

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,808,181 A (WAMSIEDLER et al) 15 September 1998 (15.09.98), see entire document.	1-3, 6-9, 11, 17-18, 20, 37-38
Y	US 5,178,763 A (DELAUNAY) 12 January 1993 (12.01.93), see entire document.	1-9

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

03 October 2002 (03.10.2002)

Date of mailing of the international search report

12 NOV 2002

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

John Kim

Telephone No. 703-308-0661